A Phase II Trial of CG 8020 and CG 2505 in Patients with Unresectable or Metastatic Pancreatic Cancer

Nontechnical Abstract

Cancer of the pancreas is the tenth leading cause of cancer in the United States with an estimated incidence of 28,300 new cases in 2000. It is also one of the most lethal malignancies and is currently the fifth leading cause of cancer death with an estimated number of deaths in 2000 similar to the incidence rate. The death rate in pancreatic cancer is exceeded only by lung, colorectal, breast, and prostate cancer. The median survival for pancreatic cancer is 15- 19 months for resectable disease, 6-9 months for locally advanced, unresectable disease, and 3-6 months for metastatic disease. All stages combined have a 1-year survival of 20% and a 5-year survival of approximately 3%. The only treatment option with the potential for cure is surgical resection. Only 20% of those diagnosed with the disease, however, have resectable disease and most of these individuals relapse despite apparent complete resection. Unresectable and metastatic disease is not curable. Only one drug, Gemcitabine, is currently approved for unresectable or metastatic disease. Although Gemcitabine is the current standard therapy for unresectable and metastatic pancreatic cancer it is only modestly active in this disease. Gemcitabine was approved by the FDA based primarily on improvement in quality of life criteria observed during a randomized study of the drug.

Given the incurable nature of unresectable and metastatic pancreatic cancer with currently available therapy, novel treatment strategies are needed. This trial will attempt to harness the power of immunotherapy by using an allogeneic tumor vaccine to fight advanced pancreatic cancer. Immunotherapy is a type of treatment for cancer based on the idea that the immune system (the system in the body that fights infection) can be activated to destroy cancer cells that have grown undetected. A vaccine is a way of delivering an antigen (something that stimulates the immune system) to the immune system so that it recognizes the antigen as foreign and destroys any cells bearing that antigen.

The vaccine used in this study, Pancreatic GVAX®, is an allogeneic pancreatic tumor cell vaccine consisting of two types of pancreatic tumor cells (CG 8020 and CG 2505) developed from the tumor cells of patients with pancreatic cancer. The human GM-CSF gene was used to genetically modify the pancreatic cells that make up the vaccine. GM-CSF is a substance made by the body that helps the immune system recognize a tumor and destroy it. The vaccine cells are irradiated to prevent them from growing or dividing. The cells themselves are **not** radioactive.

This is a Phase II clinical trial of Pancreatic GVAX® in patients with unresectable or metastatic adenocarcinoma of the pancreas. The primary objective of this trial will be to assess the safety of Pancreatic GVAX®. Secondary aims of this study will be to assess

the efficacy of Pancreatic GVAX® by measuring the clinical benefit patients might receive from the treatment (analgesic consumption, pain assessment, weight gain, and , performance status will be used to assess any possible clinical benefit), the length of time a patient experiences improvement or stabilization of his condition, how long the patient survives, and the blood levels of the tumor marker CA 19-9 which is thought to correlate with the extent of disease.

Forty patients with unresectable or metastatic pancreatic cancer will be enrolled in the trial. Treatment will consist of Pancreatic GVAX® injected into the skin six times at three week intervals. The total number of cells in each vaccination will be 50,000,000 (25,000,000 each of CG 8020 and CG 2505), divided into 8 to 16 injections, given in the thighs and arms. The choice of 8 to I6 injections for each vaccination is based on the volume of the vaccination and a finding that the body has a better chance to respond to the vaccine if it is injected into a number of different areas.

Patients will be ineligible for the trial if they have received previous cancer vaccine or gene therapy. Patients cannot receive surgery or radiation therapy within 4 wks of the first vaccination. Also, any chemotherapy must be completed at least 2 wks before the first vaccination. Patients cannot receive other cancer therapy while they are participating in this trial.

Patients will be monitored frequently throughout the trial for toxicity from Pancreatic GVAX® with laboratory testing, history and physical examination. Disease status will be followed with assessment of clinical response, radiographic studies, blood tests, and physical examination. Patients who show evidence of disease progression or excess toxicity will not continue to receive the vaccine. If significant vaccine related toxicity occurs in 30% or more patients during the trial, enrollment will be stopped. In addition, if vaccine related severe toxicity is experienced by two or more patients the study will be stopped. Responding patients will continue to receive therapy on the clinical trial until a maximum of six vaccinations have been received. Patients will be actively monitored for an additional 9 months after their last vaccination or until they begin a new treatment for pancreatic cancer. At the end of the study period patients will be enrolled in a separate study for follow up as required by FDA for all subjects participating in all gene transfer studies.